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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,903	11/26/2003	Harry M. Meade	GTC-53	2943
31904	7590	07/25/2006	EXAMINER	
GTC BIOTHERAPEUTICS, INC, C/O WOLF, GREENFIELD & SACKS, P.C. FEDERAL RESERVE PLAZA 600 ATLANTIC AVE. BOSTON, MA 02210-2206			NOBLE, MARCIA STEPHENS	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Notice of Non-Compliant  
Amendment (37 CFR 1.121)**

Application No.

10/722,903

Examiner

Marcia S. Noble

Applicant(s)

MEADE ET AL.

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

The amendment document filed on 10 May 2006 is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121 or 1.4. In order for the amendment document to be compliant, correction of the following item(s) is required.

THE FOLLOWING MARKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

- ☐ 1. Amendments to the specification:
- ☐ A. Amended paragraph(s) do not include markings.
  - ☐ B. New paragraph(s) should not be underlined.
  - ☐ C. Other \_\_\_\_\_.
- ☐ 2. Abstract:
- ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
  - ☐ B. Other \_\_\_\_\_.
- ☐ 3. Amendments to the drawings:
- ☐ A. The drawings are not properly identified in the top margin as "Replacement Sheet," "New Sheet," or "Annotated Sheet" as required by 37 CFR 1.121(d).
  - ☐ B. The practice of submitting proposed drawing correction has been eliminated. Replacement drawings showing amended figures, without markings, in compliance with 37 CFR 1.84 are required.
  - ☐ C. Other \_\_\_\_\_.
- ☐ 4. Amendments to the claims:
- ☐ A. A complete listing of all of the claims is not present.
  - ☐ B. The listing of claims does not include the text of all pending claims (including withdrawn claims)
  - ☐ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by using one of the following status identifiers: (Original), (Currently amended), (Canceled), (Previously presented), (New), (Not entered), (Withdrawn) and (Withdrawn-currently amended).
  - ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
  - ☐ E. Other: \_\_\_\_\_.
- ☒ 5. Other (e.g., the amendment is unsigned or not signed in accordance with 37 CFR 1.4):  
Sequence Compliance. CRF was not compliant. See PTO-90C and Error Report attached.

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP § 714.

**TIME PERIODS FOR FILING A REPLY TO THIS NOTICE:**

1. Applicant is given **no new time period** if the non-compliant amendment is an after-final amendment or an amendment filed after allowance. If applicant wishes to resubmit the non-compliant after-final amendment with corrections, the **entire corrected amendment** must be resubmitted.
2. Applicant is given **one month**, or thirty (30) days, whichever is longer, from the mail date of this notice to supply the correction, if the non-compliant amendment is one of the following: a preliminary amendment, a non-final amendment (including a submission for a request for continued examination (RCE) under 37 CFR 1.114), a supplemental amendment filed within a suspension period under 37 CFR 1.103(a) or (c), and an amendment filed in response to a *Quayle* action. If any of above boxes 1. to 4. are checked, the correction required is only the **corrected section** of the non-compliant amendment in compliance with 37 CFR 1.121.

**Extensions of time** are available under 37 CFR 1.136(a) only if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action.

**Failure to timely respond** to this notice will result in:

**Abandonment** of the application if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action; or

**Non-entry** of the amendment if the non-compliant amendment is a preliminary amendment or supplemental amendment.

Legal Instruments Examiner (LIE), if applicable

*Joe Winters*  
H01632

Telephone No.



UNITED STATES DEPARTMENT OF COMMERCE  
U.S. Patent and Trademark Office

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
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101722 903

EXAMINER
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ART UNIT	PAPER
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102005

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

NOTICE TO COMPLY

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Particularly, see Experimental example 38 in specification page 74 and example 40 in page 77, which contain sequences. (See attached notice to comply). Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer, from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

See enclosed pages prepared by STIC about Raw Sequences Listing Error

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcia S. Noble whose telephone number is (571) 272-5545. The examiner can normally be reached on M-F 9 to 5:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marcia S. Noble

*Gal W. W. W.*  
A01632

## STIC Biotechnology Systems Branch

### RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/722,903B  
Source: IFW16  
Date Processed by STIC: 5-16-06

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 4.4.0 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ehc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):  
U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/10/06

# Raw Sequence Listing Error Summary

## ERROR DETECTED

## SUGGESTED CORRECTION

SERIAL NUMBER:

10722,903 B

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY I\*TO SOFTWARE

- 1      Wrapped Nucleics  
    Wrapped Aminos      The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."
- 2      Invalid Line Length      The rules require that a line not exceed 72 characters in length. This includes white spaces.
- 3      Misaligned Amino  
    Numbering      The numbering under each 5<sup>th</sup> amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.
- 4      Non-ASCII      The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.
- 5      Variable Length      Sequence(s)      contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
- 6      PatentIn 2.0  
    "bug"      A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s)             . Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.
- 7      Skipped Sequences  
    (OLD RULES)      Sequence(s)      missing. If intentional, please insert the following lines for each skipped sequence:  
                                 (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)  
                                 (i)       SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)  
                                 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)  
                                 This sequence is intentionally skipped  
  
                                 Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.
- 8      Skipped Sequences  
    (NEW RULES)      Sequence(s)      missing. If intentional, please insert the following lines for each skipped sequence.  
                                 <240> sequence id number  
                                 <400> sequence id number  
                                 000
- 9      Use of n's or Xaa's  
    (NEW RULES)      Use of n's and/or Xaa's have been detected in the Sequence Listing.  
                                 Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.  
                                 In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.
- 10      Invalid <213>  
    Response      Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or  
                                 scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or  
                                 is Artificial Sequence
- 11      Use of <220>      Sequence(s)      missing the <220> "Feature" and associated numeric identifiers and responses.  
                                 Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or  
                                 "Unknown." Please explain source of genetic material in <220> to <223> section.  
                                 (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
- 12      PatentIn 2.0  
    "bug"      Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
- 13      Misuse of n/Xaa      "n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid



IFW16

## RAW SEQUENCE LISTING

DATE: 05/16/2006

PATENT APPLICATION: US/10/722,903B

TIME: 08:13:03

Input Set : A:\Revised Sequence Listing\_GTC-53.ST25.txt

Output Set: N:\CRF4\05162006\J722903B.raw

3 <110> APPLICANT: GTC Biotherapeutics, Inc.  
 5 <120> TITLE OF INVENTION: Modified Antibodies Stably Produced in Milk and Methods of  
 6 Producing Same  
 8 <130> FILE REFERENCE: GTC-53  
 10 <140> CURRENT APPLICATION NUMBER: 10/722,903B  
 11 <141> CURRENT FILING DATE: 2003-11-26  
 13 <150> PRIOR APPLICATION NUMBER: US 60/429,606  
 14 <151> PRIOR FILING DATE: 2002-11-27  
 16 <160> NUMBER OF SEQ ID NOS: 10  
 18 <170> SOFTWARE: PatentIn version 3.2  
 20 <210> SEQ ID NO: 1  
 21 <211> LENGTH: 61  
 22 <212> TYPE: DNA  
 23 <213> ORGANISM: Homo sapiens  
 26 <220> FEATURE:  
 27 <221> NAME/KEY: misc\_feature  
 28 <223> OTHER INFORMATION: IgG4 Hinge Region Nucleic Acid  
 30 <400> SEQUENCE: 1  
 31 tctgcagagt ccaaatatgg tccccatgc ccatcatgcc caggtaagcc aaccaggcc 60  
 33 t 61  
 36 <210> SEQ ID NO: 2  
 37 <211> LENGTH: 12  
 38 <212> TYPE: PRT  
 39 <213> ORGANISM: Homo sapiens  
 42 <220> FEATURE:  
 43 <221> NAME/KEY: misc\_feature  
 44 <223> OTHER INFORMATION: IgG4 Hinge Region Amino Acid  
 46 <400> SEQUENCE: 2  
 48 Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro  
 49 1 5 10  
 52 <210> SEQ ID NO: 3  
 53 <211> LENGTH: 33  
 54 <212> TYPE: DNA  
 55 <213> ORGANISM: oligonucleotide  
 58 <220> FEATURE:  
 59 <221> NAME/KEY: misc\_feature  
 60 <223> OTHER INFORMATION: S241P Oligo Nucleic Acid  
 62 <400> SEQUENCE: 3  
 63 ggtcccccatt gtcctccctg cccaggtaag cca  
 66 <210> SEQ ID NO: 4  
 67 <211> LENGTH: 11  
 68 <212> TYPE: PRT  
 69 <213> ORGANISM: oligonucleotide

Does Not Comply  
Corrected Diskette Needed  
(pg. 1, 3) 2

See item  
#10 on  
error  
Summary  
Sheet.

## RAW SEQUENCE LISTING

DATE: 05/16/2006

PATENT APPLICATION: US/10/722,903B

TIME: 08:13:03

Input Set : A:\Revised Sequence Listing\_GTC-53.ST25.txt

Output Set: N:\CRF4\05162006\J722903B.raw

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72 <220> FEATURE:
73 <221> NAME/KEY: misc_feature
74 <223> OTHER INFORMATION: S241P Oligo Amino Acid
76 <400> SEQUENCE: 4
78 Gly Pro Pro Cys Pro Pro Cys Pro Gly Lys Pro
79 1          5          10
82 <210> SEQ ID NO: 5
83 <211> LENGTH: 65
84 <212> TYPE: DNA
85 <213> ORGANISM: Homo sapiens
88 <220> FEATURE:
89 <221> NAME/KEY: misc_feature
90 <223> OTHER INFORMATION: IgG4 Hinge Region Nucleic Acid
92 <400> SEQUENCE: 5
93 cttctctctg cagagtccaa atatgggtccc ccatgcccacat catgcccagg tccgccaacc      60
95 caggc                                                                    65
98 <210> SEQ ID NO: 6
99 <211> LENGTH: 12
100 <212> TYPE: PRT
101 <213> ORGANISM: Homo sapiens
104 <220> FEATURE:
105 <221> NAME/KEY: misc_feature
106 <223> OTHER INFORMATION: IgG4 Hinge Region Amino Acid
108 <400> SEQUENCE: 6
110 Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro
111 1          5          10
115 <210> SEQ ID NO: 7
116 <211> LENGTH: 65
117 <212> TYPE: DNA
118 <213> ORGANISM: Homo sapiens
121 <220> FEATURE:
122 <221> NAME/KEY: misc_feature
123 <223> OTHER INFORMATION: IgG2 Hinge Region Nucleic Acid
125 <400> SEQUENCE: 7
126 cttctctctg cagagcgcaa atgttggtgtc gagtgccccac cgtgcccagg tccgccaacc      60
128 caggc                                                                    65
131 <210> SEQ ID NO: 8
132 <211> LENGTH: 12
133 <212> TYPE: PRT
134 <213> ORGANISM: Homo sapiens
137 <220> FEATURE:
138 <221> NAME/KEY: misc_feature
139 <223> OTHER INFORMATION: IgG2 Hinge Region Amino Acid
141 <400> SEQUENCE: 8
143 Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro
144 1          5          10
147 <210> SEQ ID NO: 9
148 <211> LENGTH: 33
149 <212> TYPE: DNA

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## RAW SEQUENCE LISTING

DATE: 05/16/2006

PATENT APPLICATION: US/10/722,903B

TIME: 08:13:03

Input Set : A:\Revised Sequence Listing\_GTC-53.ST25.txt

Output Set: N:\CRF4\05162006\J722903B.raw

150 <213> ORGANISM: oligonucleotide *Invalid Response*  
153 <220> FEATURE:  
154 <221> NAME/KEY: misc\_feature  
155 <223> OTHER INFORMATION: Oligo 2014 Nucleic Acid  
157 <400> SEQUENCE: 9  
158 gaggagcagt tccagtctac ttaccgagtg gtc  
161 <210> SEQ ID NO: 10  
162 <211> LENGTH: 11  
163 <212> TYPE: PRT  
164 <213> ORGANISM: oligonucleotide *Invalid Response*  
167 <220> FEATURE:  
168 <221> NAME/KEY: misc\_feature  
169 <223> OTHER INFORMATION: Oligo 2014 Amino Acid  
172 <400> SEQUENCE: 10  
174 Glu Glu Gln Phe Gln Ser Thr Tyr Arg Val Val  
175 1 5 10

See item  
33  
#10 on  
error  
summary  
sheet.



VERIFICATION SUMMARY                      DATE: 05/16/2006  
PATENT APPLICATION:    US/10/722,903B        TIME: 08:13:04  
  
Input Set : A:\Revised Sequence Listing\_GTC-53.ST25.txt  
Output Set: N:\CRF4\05162006\J722903B.raw